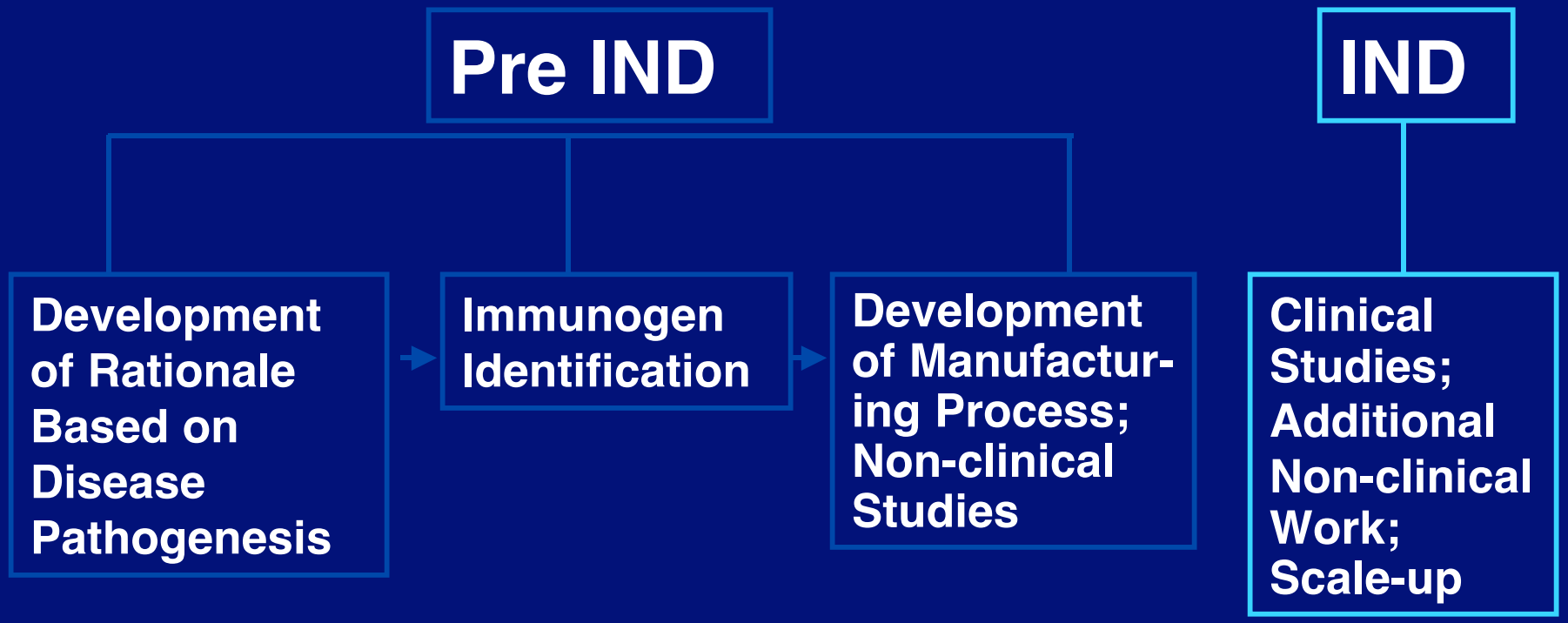
SARS Vaccine Development: An FDA Perspective

Karen Midthun, M.D.

Office of Vaccines Research and Review
CBER/FDA

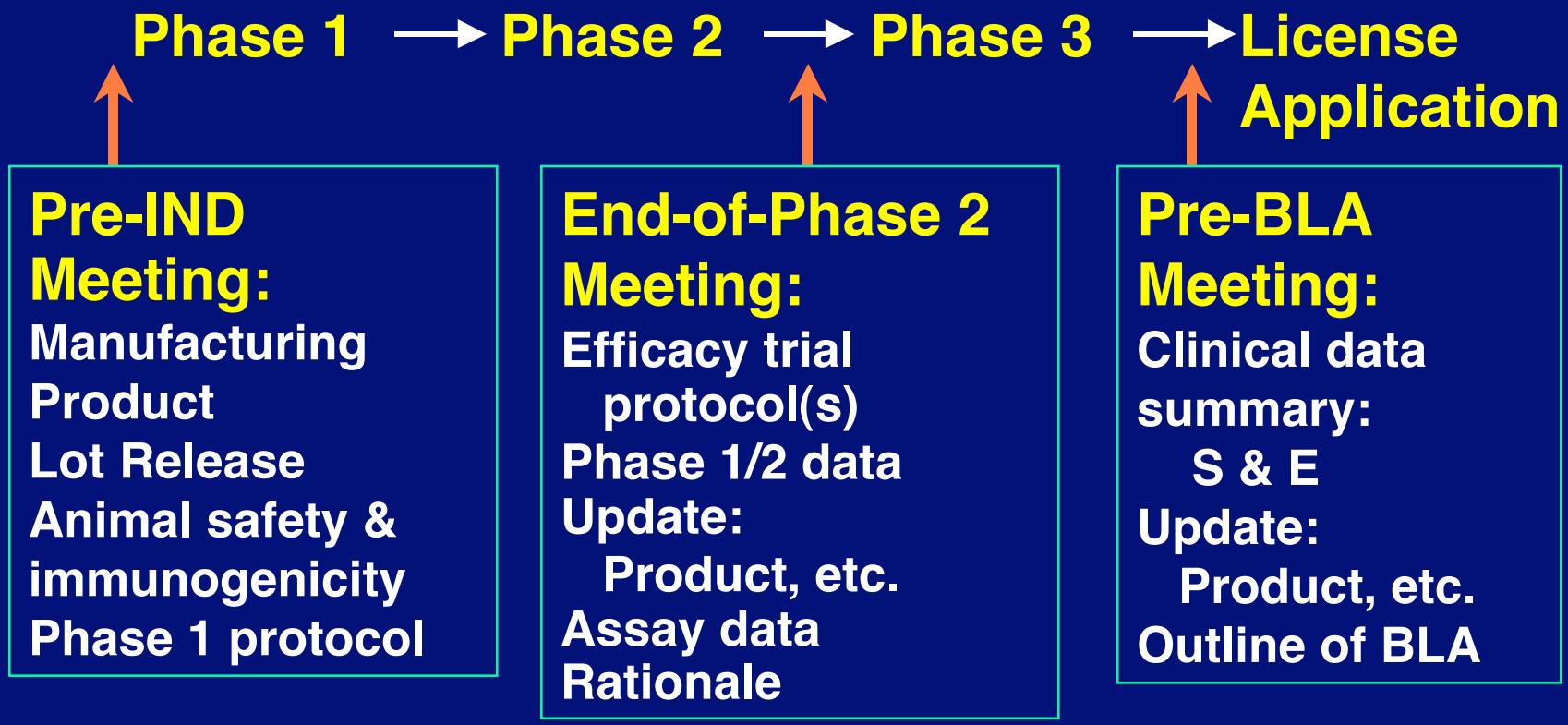
May 30, 2003

Vaccine Development



IND =Investigational New Drug application

Meetings with FDA
(21 CFR 312.47)



IND =Investigational New Drug Application
BLA =Biologics License Application

Factors to consider in selecting SARS vaccine candidates

- **Viral pathogenesis:**
  - **What is the natural history?**
  - **Routes of transmission?**
  - **Does natural infection confer protection?**
  - **How much viral strain variation occurs and will a vaccine based on a single strain or subunit thereof be protective?**
  - **Can the protective antigens be identified?**
  - **Does the virus persist/establish latency?**
  - **Who is at risk and what is the target population for vaccination?**

Considerations for vaccine type

- Live attenuated
  - Sufficiently attenuated?
  - Potential for reversion?
  - Potential for transmission?
- Inactivated
  - Adequately inactivated?
  - Are critical protective antigens/epitopes preserved?
- Subunit, recombinant
  - Have the critical protective antigens been included and presented in a way that induces protective immunity?

Viral Vaccine Production

- Source and quality of starting material
- Selection/characterization of cell substrate, e.g., identity, endogenous viruses, adventitious agents
- Viral seed history and characterization
- Validation of manufacturing process for removal and/or inactivation of viruses
- In process testing
- Release testing of bulk and final products

Non-clinical Safety Studies

- Study design predicated on intended clinica use
- Relevant animal model
- Evaluation of product specific concerns
- Safety studies conducted under GLP requirements

Non-clinical Studies to Assess Vaccine Efficacy

- Challenge/protection studies in an appropriate animal model
  - May provide rationale for use in humans
  - May provide insight into whether the vaccine-elicited immune response leads exacerbation of subsequent disease upo challenge with wild-type virus

Clinical Development under IND

- Phase 1: safety and immunogenicity
- Phase 2: safety, immunogenicity, dose ranging
- Phase 3: efficacy, safety, immunogenicity
  - Can an efficacy trial be conducted? If feasible, will provide best information on efficacy and potential for immunopathogenesis caused by vaccination.
  - Validated assays need to be developed to measure immune responses and also to diagnose disease as pa of case definition.
  - If efficacy trial not feasible, are there appropriate anima models that could be used in support of efficacy?

Vaccine Development: FDA Resources

- **OVRR is ready to**
  - **Provide guidance on manufacturing concerns (e.g. up-front recommendations for cell substrates)**
  - **Provide guidance on animal studies (both for non-clinical safety and efficacy evaluations)**
  - **Assist/collaborate/facilitate the development of assays required for vaccine characterization and evaluation of vaccine-induced immune responses**
  - **Provide guidance on clinical trial design**

Vaccine Development: Conclusions

- Vaccines have unique considerations for product & clinical development
- Overall planning and coordination:
  - Product characterization & manufacturing (cGMP)
  - Non-clinical studies
  - Anticipate needs of future trials, e.g., critical assay
  - Accumulate sufficient safety, immunogenicity & efficacy data during development
  - Clinical bridging studies, e.g., population; product scale-up
  - Prospective application of Good Clinical Practices
- Utilize available FDA documents/resources

Guidance Documents - Examples

- FDA Guidance for Industry
  - Content and Format of Chemistry, Manufacturi Controls Information and Establishment Description Information for a Vaccine or Relate Product (1999)
- ICH Guidance Documents
  - Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin (1998)
  - Quality of Biological Products: Derivation and Characterization of Cell Substrates (1998)

Available Resources

- FDA documents /Federal Register (FR) notices /FDA regulations
  - http://www.fda.gov/cber/publications.htm
  - 1-800-835-4709 or 301-827-1800
- International Conference on Harmonisation (ICH) Documents (U.S., E.U. and Japan)
- Parkman P, Hardegree MC: Regulation & Testing of Vaccines. Vaccines 3rd ed, 1999, WB Saund